REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments. Claims 1-18 were pending. By this Amendment, claims 1-18 have been amended. It is believed that no new matter has been added. Accordingly, claims 1-18 are pending.

Objection to the specification

Amendments have been made to the specification to correct grammatical and spelling errors.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claim 2-6, 10, 11, and 16-18 under 35 U.S.C. § 112, written description, enablement

The claims do not require knowing each and every antibody (as the Examiner seems to suggest). Rather the claims just relate to the identification of elastases and furthermore it is believed that it is known in the art to obtain antibodies for every known elastases.

The Examiner points out that different combinations of heavy and light chains can result in different antibodies having the same specificity and no guidance is given what structure is important for their function. However, if a higher organism (e.g. a vertebrate) is invaded by an antigen, the immune system produces, in regular, a repertoire of different cells (e.g. antigen presenting cells) and antibodies (e.g. IgG, IgA, IgD, IgE, IgM), thus dependend on the sort of antigen and the duration of the infection, both of which are usually known or predictiable. Further, the common structures of antibodies are well known to the person skilled in the art and include common structural features: The basic unit of each antibody is a monomer. An antibody can be monomeric, dimeric, trimeric, tetrameric, pentameric etc. The monomer is a "Y"-shaped molecule that consists of two identical heavy chains and two identical light chains connected by disulfide bonds. Each heavy chain has a constant region, which is the same by all immunoglobulins of the same class, and a variable region which differs between immunoglobulins of different B cells, but is the same for all immunoglobulins produced by the same B cell.The variable domain of any heavy chain is composed of one domain. These domains are about 110 amino acids long.Each light chain of the antibody has two successive domains: one constant and one variable domain. The approximate length of a light chain is from 211 to 217 amino acids.

Each half of the forked end of the "Y" shaped monomer is called the Fab (*f*ragment *b*inding *a*ntigen) fragment. It is composed of one constant and one variable domain of each the heavy and the light chain, which together shape the antigen binding site at the amino terminal end of the monomer. The two variable domains bind the

antigens they are specific for and that elicited their production.The main reason that the human immune system is capable of binding so many antigens is the variable region of the heavy chain.

Hence it can be concluded, that it is known to the person skilled in the art, what antibody structure is important for their function.

The claimed invention relates to a heterogenous population of different antibodies providing different paratopes and different paratope structures. It seems questionable, if, at all, the structure of a paratope could be reliably described by a structure. X-ray structures can only provide a snap shot of a paratope region having rotational and lateral degrees of freedom i.e. wagging and wobbling motions, which furthermore change their conformation in contact with the antigen.

The results obtained by the use of the disclosed antigens for producing antibodies was clearly unpredictable, because in general the immmunization of an animal by an antigen is an empirical art, in which the routineer is unable to foresee what particular antibodies will be produced and which specific amino acids of the antigen will be recognized by them.

In conclusion, the antibodies according to the claimed invention are defined by their general structure, by their paratope region specific to the antigen used, and their functionality for enabling the claimed inventive procedure.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claim 1-11 and 16-18 under 35 U.S.C. § 112, indefiniteness

The claims have been amended. In respect to claims 10, 11, and 16, it is believed that they are in proper dependent form now as claim 7 has been amended.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claims 12-15 under 35 U.S.C. § 101

Claims 12-15 have been amended, which now recite ""synthetic" before peptide.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claims 1-8, 10, and 12-18 under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al.

In order to show anticipation, the reference must teach or suggest every element of the claimed invention.

The Examiner points out that Sziegoleit et al. discloses a sandwich immunosorbent assay for pancreatits or pancreatic cancer by determining pancreatic elastase 1 using polyclonal antibodies.

Sziegoleit et al. describes a method using whole elastase 1 (E1) being isolated from necrotic organs, immunizing rabbits and sheeps by the use of E1, isolating antibodies by affinity chromatography using immobilized E1, coupling the antibodies to the cavities of a microtiter plate and performing an ELISA for detecting elastase 1 in the serum of patients suffering from pancreatitis (see page 79).

However, no isoform of elastase is mentioned in Sziegoleit et al. Furthermore, no specificity of the resulting antibodies against elastase 1 is proven, since no saturation curve is visible in Figure 2, when immobilized antibodies are incubated with different concentrations of dissolved E1. Beyond this, only 6-7% of the enzyme in serum is immunoreactive (page 81, first column, second paragraph).

In contrast, the invention relates to a diagnostic procedure by determining the overall content of all known pancreatic elastase isoforms (see claim 1), thus allowing for the first time a simple and highly sensitive recognition of pancreas function disorders, also in secretions and excretions of a patient. The latter was totally surprisingly found and was not expected by the inventors, revealing the advantageous characteristics of the invention.

The peptides used for immunization are derived from different isoforms, e.g. from **elastase 3** (A-V-K-E-G-P-E-Q-V-I-P-I-N, Y-T-N-G-P-L-P-D-K-L-Q-Q-A-R, R-S-G- C-N-G-D-S-G-G-P-L-N, G-P-L-N-C-P-T-E-D-G-G-W-Q, S-L-Q-Y-E-K-S-G-S-F-Y), **elastase 1** (G-T-E-A-G-R-N-S-W-P-S-Q-I, H-N-L-S-Q-N-D-G-T-E-Q-Y-V, W-G-K-T-K-T-N-G-Q-L-A, V-S-S-R-G-C-N-V-S-R-K-P-T), **elastase 2** (G-G-E-E-A-R-P-N-S-W-P-W-Q, S-S-S-R-T-Y-R-V-G-L-G-R-H-N, K-D-W-N-S-N-Q-I-S-K-G-N-D, G-P-L-N-C-

Q-A-S-D-G-R-W, G-A-L-P-D-D-L-K-Q-G-R-L), **elastase 1** and **3** (F-G-C-N-T-R-R-K-P-T-V-F-T), or from the elastase 1-3 precursors.

As being disclosed in the description of the invention, the specificity of the resulting antibodies and their sensitivity towards elastase samples from stool and pancreatic juice is demonstrated, e.g. elastase can be detected in all samples with individual antibodies or antibody mixtures, but not every antibody detects all isoforms (Example 5).

Thus, Sziegoleit et al does not anticipate the claimed invention because Sziegoleit et al fails to teach or suggest every element of the claimed invention.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claims 1-8 and 10-18 under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al.

The Examiner stated that Scheefers et al., discloses the determination of pancreatic elastase 1 in serum and stool samples by antibodies elicited to different epitopes of the protein as indicative of pancreatic disease.

It is believed that Scheefers et al. (US 5622837) discloses the use of only one antigen (T-M-V-A-G-G-D-I-R) for achieving antibodies against elastase 1.

The sequence T-M-V-A-G-G-D-I-R is artificial because it is believed, at present-day, not findable in any elastase or any other known protein (see *ExPASy Blast* and *Entrez Protein* databases). However, partially this sequence is related to T-M-V-C-A-G-G-D-I-R of elastase 3, but no connection to elastase 3 is disclosed in Scheefers et al.

Since no alignment or the use of computer programs is mentioned in Scheefers et al., it remains unclear, wherefrom the used antigen sequence has been achieved or derived.

In contrast, the claimed invention uses peptides, being derived as linear epitopes from all known elastase isoforms (see claim 1).

Thus, Scheefers does not anticipate the claimed invention because Scheefers fails to teach or suggest every element of the claimed invention.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefore. The Assistant Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

CONCLUSION

Based on the foregoing remarks it is believed that the claim is in condition for allowance.

Respectfully submitted,

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